

### **REMARKS**

The Examiner is thanked for issuing the outstanding Action as a non-final Action.

We note that although a claim set was submitted for the Examiner's convenience in the prior Response dated November 21, 2007, it did not present any amendments to the claims at that time.

#### **Interview Summary**

The undersigned thanks Examiner Michael C. Henry and Supervisory Examiner Shaojia A. Jiang for the courtesies extended during the telephonic Interview held on May 21, 2008. Although the undersigned presented arguments in favor of patentability of the claims, the Examiners were not persuaded.

#### **Obviousness Rejection**

Claims 31-33 and 37-47 were rejected under 35 USC § 103(a) as obvious over Cantor US Patent No. 5,633,003 ("Cantor") in combination with Green WO 96/19968 ("Green"). (Paper No. 20080216 at 2.) The Examiner has set forth in the present Action on pages 2 to 5 the arguments as in the prior Action dated May 22, 2007 (Paper No. 20070514 at 2-6.) These arguments of the Examiner have been summarized in the prior Response dated November 21, 2007 on pages 7-8.

Arguments on behalf of Applicants submitted on the record thus far are incorporated here as if presented in full.

In the "Response to Arguments" section of the present Action, the Examiner asserted that "[t]he applicant argues that Applicants have found that the lowest molecular weight hyaluronic acid, 227 KDa, had the best properties of the three tested in terms of elastic fiber protection and optimum aerosol particle size. (Id. at 51-61). Cantor's report, on the other hand, of naturally occurring, polydisperse hyaluronic acid, provides no teaching, suggestion or motivation to one of ordinary skill in the art to achieve a system comprising a mixture having a polysaccharide of the recited molecular weight range that encompasses a polysaccharide of a defined molecular weight within the recited range." (Id. at 6.) The Examiner asserted, however, that "Cantor suggests that hyaluronic acid from different sources (i.e., hyaluronic acid from bovine sources, rooster comb, human umbilical cord, or streptococcus zoepidicus (see col. 3, lines 13-18) which are known to have different molecular weights can be used [and that] one of ordinary skill in the art would be motivated to determine the most effect aerosol form of the hyaluronic acid composition that is administered to a patient." (Id.)

The Examiner further asserted that "[t]he applicant argues that one skilled in the art would not have considered a system adapted for delivery of a formulation to a respiratory tract of a mammal comprising a polysaccharide having a molecular weight as recited in the present claims." (Id.) The Examiner asserted, however, that "Cantor (the reference used in the above rejection) discloses that hyaluronic acid (in general) can be delivered in an aerosol form using a nebulizer (the same device or system used by applicant)." (Id.)

In addition, the Examiner asserted that "[t]he applicant argues that Green, in reporting on the use of the "particular sugars" which are the single unit sugars of low

molecular weight, tends to lead one of skill in the art away from the use of the polysaccharides as presently claimed. However, because Green reports that sugars (i.e., carbohydrates) can be used in aerosol formulation and Cantor disclose that the polysaccharide hyaluronic acid can be used in aerosol formulation, then one of skill in the art would be lead [sic] to use of the polysaccharide (which a [sic] carbohydrate) as presently claimed." (Id. at 6-7.)

Furthermore, the Examiner asserted that "[t]he applicant argues that Green is concerned with aerosol formulations for use in the administration of a drug by inhalation (Green, pg 1, In 3-4). However, Green discloses that fluorocarbons can be used and are commonly used as propellants for medicinal aerosol formulations (see page 1, lines 6-21, especially lines 16-21) which implies that fluorocarbons can be used as propellants for drugs or medicinals such as cantor's areosol [sic] hyaluronic acid. It should be noted that Green, like Cantor, also uses the same method of delivery (aerosol inhalation) for the same purpose (i.e., treating respiratory disorders)." (Id. at 7.)

It is respectfully submitted that the Examiner has erred in failing to consider the Horton (Horton M. R., *et al.*, Induction and Regulation of Macrophage Metalloelastase by Hyaluronan Fragments in Mouse Macrophages. *J. Immunol.* 1999;162: 4171-4176) and McKee (McKee C. M., *et al.*, Hyaluronan (HA) Fragments Induce Chemokine Gene Expression in Alveolar Macrophages. The Role of HA Size and CD44. *J. Clin Invest.* 1996; 98: 2403-2413) art that was submitted with a Supplemental Information Disclosure Statement with the prior Response and which was addressed in the arguments of the prior Response on pages 10-12. The Examiner made no mention of Horton or McKee or of the arguments made in the prior Response

referencing this art in the "Response to Arguments" section of the Action on pages 6-7, or indeed, anywhere in the present Action at all. As is well established in the law, "[o]n the issue of obviousness, the combined teachings of the prior art as a whole must be considered." *EWP Corp. v. Reliance Universal, Inc.*, 225 USPQ 20, 25 (Fed. Cir. 1985). In view of the Examiner's error, the rejection must be withdrawn for this reason alone.

We have argued that art subsequent to Cantor (the patent cited in the present rejection) reports that low molecular weight hyaluronic acid (e.g., less than 250 kDa) may be pro-inflammatory. Cantor was filed in 1994 and issued in 1997. Horton and McKee published in 1999 and 1996, respectively. Following the publication of Horton in 1999, one skilled in the art would recognize at least these two reports evidencing a pro-inflammatory response associated with low molecular weight hyaluronic acid.

It is incumbent on the Examiner to consider such evidence in the art, as it detracts from a suggestion in Cantor, if any, to attain the claimed system which is adapted for delivery to a respiratory tract of the recited polysaccharide which has utility in treating or ameliorating the symptoms of a respiratory disorder. Furthermore, in view of Horton and McKee, one skilled in the art would be led away from the presently claimed invention. As noted, the Examiner must consider such evidence. Even when there may be a situation where certain documents could be considered to conflict with the teachings of certain other documents, the Examiner must "consider all disclosures of the prior art [and,] in weighing the suggestive power of each reference, must [take into account] the degree to which one reference might accurately discredit another." *In re Young*, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991). Again, the law requires

consideration of the "whole" of the prior art. *In re Keller*, 208 USPQ 871, 881 (CCPA 1981).

During the Interview with the Examiners, the arguments concerning Horton and McKee were presented. The Examiners responded that the "side effect" of a pro-inflammatory response implicated by Horton and McKee are of no moment to overcome the obviousness rejection. We respectfully submit that the Examiners have erred in their characterization of Horton and McKee in the Interview. A **pro-inflammatory response in the airways** in connection with a system **for inhalable delivery** of the recited polysaccharide, the utility of which is **for treating or ameliorating the symptoms of a respiratory disorder**, is not fairly characterized as a "side effect," but rather, is in contradiction with the very purpose of the claimed system.

Motivation to attain the claimed invention based on Cantor is lacking as Horton and McKee indicate that the claimed system for inhalable delivery of the recited polysaccharide for treating or ameliorating the symptoms of respiratory disease would become inoperable or have its intended function obliterated in view of a pro-inflammatory response as disclosed by Horton and McKee. See *In re Fritch*, 23 USPQ2d 1780, 1783 n12 (a rejection is inappropriate when a reference renders the modification suggested by the Examiner inoperable for its intended purpose); *In re Haruna*, 58 USPQ2d 1517, 1522 (Fed. Cir. 2001) (the Board's conclusion ignored teachings in the reference that discourage a disk with the claimed assembly, and thus, the reference taught away from the claimed assembly).

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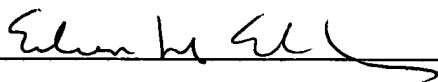
It is submitted that in view of the art as a whole, the rejection must fall.

Reconsideration and withdrawal of the rejection are respectfully requested.

It is believed that the present application is in condition for allowance.

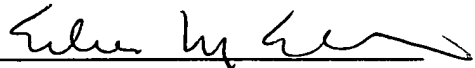
Issuance of a Notice of Allowance is requested.

I hereby certify that this correspondence is being mailed to the United States Patent Office to the Mail Stop Amendment Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450 on August 21, 2008.



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Respectfully submitted,

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